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510(k) Summary of Safety and Effectiveness

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Ventana Medical Systems' Anti-Human Melanosome(Clone HMB45) may be used to aid in the identification of abnormal cells of melanocytic lineage as an aid in diagnosis of anaplastic tumors. Anti-Human Melanosome(Clone HMB45) specifically binds to an oncofetal antigen present within immature melanosomes in the cytoplasm of melanoma cells and prenatal and infantile epithelium. This product is substantially equivalent to the same clone sold by a different manufacturer.

Ventana Medical Systems' Anti-Human Melanosome(Clone HMB45) contains a mouse monoclonal antibody directed against a 10kD neuraminidase sensitive sialylated glycoconjugate present in immature melanosomes[1]. Melanoma metastases from axillary lymph node finely minced in phosphate buffered saline was used as the immunogen. The spleen from a BALB/c mouse injected intraperitoneally with the minced tissue was fused with NS-1 cells. Hybridomas were screened by immunocytochemistry on Carnoy's fixed, paraffin-embedded sections of the same melanoma that was used as an immunogen[2].

In normal tissues, HMB45 has been shown to react with immature melanosomes in fetal and neonatal melanocytes and infantile retinal pigment epithelium[1,2]. It does not react with normal resting adult melanocytes, regardless of the degree of pigmentation[2,3,8]. The presence of the antigen indicates active melanosome formation and thus melanocytic differentiation[9,13]. Adult melanocytes are capable of re-expressing the fetal antigen upon activation. Melanocytes activated by a variety of stimuli have been observed. For example, HMB45 positive cells have been detected in tissue overlying or adjacent to granulation tissue, hemangiomas, vessel-rich tumor stroma, and basal cell carcinomas[3,9,10,13]. Occasional pigmented cells of hair follicles have been observed to stain positively[2]. HMB45 staining has not been observed with melanocytes in lentigines or overlying fibroblastic proliferations, such as keloids, dermatofibromas and old fibrotic hemangiomas[9]. HMB45 does not appear to react with any non-melanocytic tissues, and its expression in adults is confined to neoplastic melanocytic cells[1].

Many fetal antigens are re-expressed in oncogenic tissue. In malignant cells, HMB45 stains most primary and metastatic melanomas[2,3,4,5,8,13]. Several investigators have confirmed the high sensitivity and specificity of HMB45 for melanoma[3,4,5]. Desmoplastic malignant melanomas infrequently express the HMB45 antigen, possibly because they contain few melanosomes and have a mesenchymal pattern of differentiation[2,13]. Non melanocytic tumor cells of epithelial, lymphoreticular, glial and mesenchymal origin are not labeled[1,3,4], except for renal angiomyolipomas (RAML), a type of mesenchymal hamartoma[11,12]. An HMB45-related antigen located in the myoid component of RAML appears to be similar to the HMB45 antigen present in melanomas[12].

HMB45 is reactive with "activated" melanocytes as seen in melanomas, junctional nevi, junctional components of compound nevi, Spitz nevi, and cellular blue nevi, while it is nonreactive with common acquired and intradermal nevi and intradermal components of compound nevi[2,3,6,13]. Because of this differential staining on pigmented cells, HMB45 immunostaining may be a

useful adjunct for measuring the Breslow depth of melanomas, since it is positive on melanoma cells and negative on deep nevi cells that may accompany melanomas[6,7]. Unfortunately, HMB45 is not useful in distinguishing benign and malignant melanocytic proliferation because it recognizes junctional nevi, Spitz tumors and atypical melanocytic hyperplasia[2].

Comparative Study

Supporting data for the equivalence statement is shown by the following study. Formalin fixed paraffin embedded preparations from normal and pathologic samples were tested using the Ventana Anti-Human Melanosome Antibody. Samples were obtained from excess tissues obtained for reasons other than the present study. Pathologic and normal tissues were examined. Slides were processed on the Ventana ES Automated Slide Stainer, prepared for examination, and evaluated by a qualified pathologist for specific staining intensity and background staining.

Results

Staining occurred in the cytoplasm of melanoma cells. Negative control tissue was all negative. There was no inappropriate staining of the tissues in this study.

Specificity of the antibody was shown by no staining of normal cells of 75 normal tissues and staining of cells of melanoma tumors.

The sensitivity of this antibody was shown by consistent staining of 19 of 20 melanoma tumors. This agrees with the report Gowan and associates[2] where 60 of 62 melanomas showed positive staining. As with any immunohistochemical reagent, the sensitivity is dependent on tissue processing and slide preparation parameters. The negative control which was run with each tissue gave negative results.

Inter-run reproducibility was determined based on samples of the same tissue on 16 different instrument runs using the antibody and DAB detection kits. Sixteen of 16 stained positively. All slides has similar staining intensity. Intra-run reproducibility was determined based on 10 samples of the same tissue within one run using the antibody and DAB detection kits. Ten of 10 slides stained positively. All slides stained with equivalent staining intensity.

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